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Comparing Cognitive Functioning and Adverse Metabolic Effects of Consumers Taking Type 1 or Type 2 Antipsychotic Medications with Un-medicated Consumers

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Abstract

Obesity and metabolic side effects such as diabetes mellitus are major concerns in public health. Mentally ill people are a high risk subgroup for obesity and metabolic syndrome because of behavior, non treatment, and medication side effects. In this research, I conducted a retrospective chart review to compare the weight and body mass index of consumers who were prescribed antipsychotic Type 1 or Type 2 medications. The sample was drawn from consumers attending the Consumer Advocacy Model (CAM) program which is an outpatient substance abuse and mental health treatment program in the Wright State University Boonshoft School of Medicine Department of Community Health.

The primary aim of the study was to evaluate this local clinical population and make recommendations in the context of upcoming universal health coverage plan for prescribing antipsychotic medications. This is based on lowering the cost and increasing effectivity of medication use in treatment for this population.

Method: Medical charts of 195 patients seen at the Consumer Advocacy Model (CAM) Urbana, Ohio location were reviewed, and this data was analyzed. A review of other patients 'subjective experiences were also gathered from the Consumer Health Resource Group, (Consumer Health Reports, 2011).

Results: During a period of four months, 42 patients were prescribed risperidone; 59 were prescribed olanzapine; 53 were prescribed Seroquel; and 46 were prescribed three other antipsychotics. The predominant adverse effects produced by most of the antipsychotic Type 2 drugs consisted of weight gain and sedation.

Conclusion: This data analysis raises awareness that obesity is a major health risk factor with the use of Type 2 antipsychotic drugs. Suggestions for identifying expected weight gain in the consumers as well as addressing negative health consequences of obesity are discussed.

Introduction and Literature Review

During the 1950's the first antipsychotic medication was discovered. Antipsychotics are broadly divided into two groups, the typical or Type 1 or first-generation antipsychotics and the atypical or Type 2 or second-generation antipsychotics. The Type 1 antipsychotics are classified according to their chemical structure while the Type 2 antipsychotics are classified according to their pharmacological properties.

Antipsychotic drugs are prescribed with increasing frequency to people with an expanding variety of diagnoses such as schizophrenia, schizoaffective disorders, bipolar disorders, and schizophreniform disorders (Brannon, 2011). Early investigators noted the striking ability of the first such drugs to produce a patient state characterized by mental slowing, apathy, and emotional indifference (Moncrieff, Cohen, & Mason, 2009). Subsequent studies with volunteers and first person accounts by patients also emphasize the emotional detachment, reduced initiative, dysphoria, and akathisia produced by these drugs. Over the years, various labels have been used to describe these effects, including neuroleptic induced dysphoria, akinetic depression, neuroleptic induced deficit syndrome, and behavioral toxicity (Challoner, 2010).

An antipsychotic is a tranquilizing psychiatric medication primarily used to manage psychosis. Many physicians are now prescribing the Type 2 antipsychotic medications for schizophrenia and bipolar disorders, and this has led to increased risk for diabetes mellitus and the development of metabolic syndrome, which can present as weight gain, hypertriglyceridemia, as well as increased insulin, glucose and low-density lipoprotein cholesterol levels (Zagaria, 2011). Treatment with Type 2 antipsychotics may increase the risk of metabolic syndrome and diabetes (Lieberman, 2004a; Newcomer, 2007).

The right balance of treatment for schizophrenia in terms of risks versus benefits is very important and current professional guidelines for these medications recommend that Type 1 antipsychotic medications have the same efficacy as Type 2 but do not lead to obesity (Mandell, Unis, & Sackett, 2011). There is also short term versus long term cost benefit for the use of Type 1 antipsychotic medications rather than Type 2 medications which are expensive for the consumer to use.

Obesity and Metabolic Syndrome are Public Health Problems

Obesity and complex metabolic syndrome,which includes insulin resistance and diabetes mellitus, are major public health issues. Obesity is increasing substantially and is one of the major contributors of disease prevalence due to its pathophysiological link to other cardiovascular risks such as hypertension and diabetes. According to the World Health Organization's recent update, diabetes, hypertension, and obesity are among the top five continuing risk factors for cardiovascular deaths in the world (Motlagh, O'Donnell, & Yusuf, 2009). It is estimated that in 2010, 6.4% of adults had diabetes mellitus affecting 285 million in the world and it is expected to increase to 7.7% by 2030, affecting 439 million adults (Shaw, Sicree, & Zimmet, 2010). Of special note is the expected 67% increase in the prevalence of diabetes in developing countries by 2030 (Shaw et al., 2010).

In a metanalysis using data from 1.46 million adults, Berrington de Gonzalez and colleagues (2010) further confirmed that overweight and obesity significantly increases the risk of mortality. The analysis pooled together data from 19 prospective studies that followed participants an average of 10 years and found that as BMI increased above the normal range (BMI = 18.5 - 24.9), the risk of premature death increased. Those in the obese category (BMI = 30 - 34.9) had a 44 percent higher risk than normal, while those with a BMI of 40 - 49.9 had

more than double the risk of premature death. Perhaps the most notable finding from this research is the sustained increase in mortality seen in the overweight category (BMI = 25 - 29.9), something not found in some previous large studies (Dart & Colditz, 2010).

Use of Antipsychotics and Obesity Statistics

In 2009, IMS Health estimates that U.S. consumers filled 52 million prescriptions for atypical antipsychotic medications, which account for the vast bulk of antipsychotic medications prescribed today (Healy, 2011). A consensus panel for monitoring the metabolic effects of Type 2 antipsychotic medicationsnoted at 10 weeks of treatment with an atypical antipsychotic medication for schizophrenia or psychotic disorder that there was an estimated average weight gain with drug treatment compared with a placebo. The weight gain varied from 0.5 to 5.0 kg with the use of Clozapine, Seroquel, Risperidone, Olanzepine, Abilify@, and Geodon (Barrett, 2004).

Effects of Obesity on the General Population

Nearly one-third (32.9%) of U.S. adults are obese (nearly 72 million adults) (Ogden, Lamb, Carroll, & Flegal, 2010). Obesity is a social stigma and has a great public health impact (Puhl & Heuer, 2010). Additionally, obese and overweight people are very likely to experience discrimination in a variety of forms (Levi, Vintner, Richardson, St. Laurent, & Segal 2009). Obesity has very serious effects on physical health. Some examples are given in the Table 1.

Healthy People 2020 Goals

Despite national efforts, obesity is still a major public health problem. As a public health problem, obesity is addressed in Healthy People 2020 goals. The goals for 2020 include reducing obesity by 10 percent. (Healthy People, 2011).

Obesity rates have recently reached 30 percent in some states, according to the Centers for Disease Control and Prevention (2010). However, chronic diseases that are highly preventable, such as heart disease and diabetes, that are directly linked to obesity are still responsible for seven out of every 10 deaths among Americans each year and account for 75 percent of the nation's health spending (Healthy People, 2011).

Cost and Economic Burden of Obesity

The annual medical costs of obesity in the United States were estimated to amount to 75 billion dollars in 2003 (Finkelstein, Ruhm, & Kosal, 2005) and responsible for between 4.3% and 7% of total health care expenditure. It is worth noting that the annual revenues for all antipsychotic drugs are $14.6 billion (Wilson, 2009).

Dart and Colditz (2010) examined the relationship between the obesity trend and increases in US health expenditures. They found that the combination of rising obesity prevalence and increased spending among the obese accounts for 27% of the growth in US health care expenditure between 1987 and 2001. The latter effect signifies the changes in standard care for diabetes, hypertension, hyperlipidemia, and heart disease (Dart & Colditz, 2010).

Thompson, Edelsberg, Kinsey, and Oster (2010) estimated absenteeism in the US due to obesity cost employers $2.4 billion in 1998. The estimated workday loss among the very obese (BMI $\geq$ 40 or BMI $\geq$ 35 and with comorbidities) derived from the 2002 National Health Interview Survey amounts to approximately four days per year for men and 5.5 days per year for women (Finkelstein et al., 2005).

Mental Illness, Physical Activity and Obesity

With obesity at epidemic levels, it is the second leading cause of preventable death in the United States because of its association with cardiovascular disease (Evans, Renaud, Finkelstein, Kamerow, & Brown, 2006). The prevalence of excess weight is even higher among adults with severe mental illness, and many of these adults have other chronic conditions such as diabetes, heart disease, hypertension, or pulmonary disease (Jones et al., 2004). Obesity is significantly associated with the use of antipsychotic medications for any mood disorder, major depressive disorder, any anxiety disorder, and most strongly with some individual anxiety disorders such as post-traumatic stress disorder (PTSD) (Scott, McGee, Wells, & Oakley Browne, 2008).

Weight gain is seen with the use of Type 2 antipsychotic medications (Ascher-Svanum, 2005). During the CATIE (Clinical Antipsychotic Trials of Intervention Effectiveness) trial , patients taking olanzapine gained an average of 0.9 kg per month. Patients taking quetiapine and risperidone showed minimal weight gain (0.5 kg and 0.36 kg increase from baseline, respectively), and those taking ziprasidone experienced weight loss (-0.72 kg) (Liberman, 2004a). To minimize weight gain and metabolic effects, it's suggested to use Abilify, Latuda, Saphris, or Geodon but not Zyprexa, clozapine, or Seroquel (Shaw et al., 2010).

Obesity can be an obstacle to adherence to medication, as evidenced by a mail survey of persons with schizophrenia where BMI status and subjective distress from weight gain were predictors of noncompliance (Citromea & Vreeland, 2009). Sometimes patients complain about the weight gain and these side-effects can be removed by simply reducing the patient's antipsychotic drug dosage or by switching the medication; unfortunately, such reduction in drug dosage or switching to another medication often causes patients to relapse back into psychosis (Grohl, 2010). The quality of life associated with schizophrenia ranks among the worst of any

chronic medical illness, and treatment with atypical antipsychotics may improve the quality of life for many of these patients (Liberman, 2004b).

In the third quarter of calendar year 2010 (July-September 2010), the Centers for Medicare and Medicaid (CMS) reports that nationwide 39.4% of nursing home residents who had cognitive impairments and behavior problems but no diagnosis of psychosis or related conditions received antipsychotic drugs (CMS, 2010). It has been reported that approximately one-quarter of nursing home residents, nearly 350,000 people , take antipsychotic drugs (Wilson, 2009; Ray et al., 1993). With the use of antipsychotic medications additional side-effects of obesity are being added to the consumers' guidance information issued by CMS (2011) which encourages facilities to use non-pharmacological alternatives and identifies situations where antipsychotic medications are not indicated.

In a study by NIMH (2008), effects of Type 2 antipsychotic medications were studied in children and adholescents. This study covered 272 patients visiting clinics from 2001 to 2007. Fifteen patients who stopped taking their medicine were used as a control group. The weight for the control group stayed level. The 257 patients who stayed on their drugs took detailed tests, including a fasting blood test to check for metabolic markers for obesity which can presage adult obesity, hypertension, and Type II Diabetes Mellitus. The metabolic markers included glucose, insulin, triglycerides,and cholesterol (Wilson, 2009). Their mean weight at the start of the study period was 118 pounds. But after about 11 weeks, those who took Zyprexa had gained 18.7 pounds; Seroquel, 13.4 pounds; Risperdal, 11.7 pounds; and Abilify, 9.7 pounds. Their waists typically expanded three inches with Zyprexa, and two inches with the other medications. All but Abilify showed rapid and significant increases in one or more metabolic markers. A similar study saw weight gain in adults with the use of antipsychotic medications predominantly

Zyprexa and risperidone for a 10 week period (Nauret, 2009). It has also been demonstrated that even untreated patients suffering from schizophrenia are at an increased risk of developing medical conditions associated with metabolic syndrome (Gautam & Meena, 2011; Lieberman, 2004b).

Regular physical activity is one of the few health behaviors with demonstrated benefits for weight loss as well as related conditions such as hypertension, cardiovascular disease, and diabetes (DHHS, 2008a; DHHS, 2008b). Physical activity levels in adults with severe mental illness are not well studied, although available evidence suggests this group is less active than the general population (Daumit, 2010). Psychological symptoms and low cognitive functioning may also pose a barrier to regular physical activity as evidenced by a previous study which found that adults with intellectual disabilities had higher levels of physical inactivity compared to the general population estimates of physical activity (Robertson et al., 2000). Additionally, persons with mental illness report that negative affective states (e.g., sadness, depression) as well as mental illness symptoms are barriers to their participation in physical activity (McDevitt, Snyder, Miller, & Wilbur, 2006; Ussher, Stanbury, Cheeseman, & Faulkner, 2007).

Risk of Developing Diabetes with Antipsychotic Medication

Use of Type 2 antipsychotic medications are problematic compared to the use of Type 1 antipsychotic medications which are associated with less incidence of metabolic syndrome (Lieberman, 2004a). For individuals with co-occurring heart disease or diabetes, this issue is of particular importance, especially when the patients present for treatment (Sicras-Mainar, Navarro-Artieda, Rejas-Gutierrez, & Blanca-Tamayo, 2008).

In a multicenter randomized prospective study, Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE), 1493 patients with schizophrenia were randomized to

receive typical antipsychotic, perphanazine, or the atypical antipsychotics, olanzapine, quetiapine or risperidone for 18 months or until discontinuation due to tolerability failure by the patients. In this study, olanzapine was associated with the greatest degree of weight gain, estimated at 0.9 kg/month and an increased fasting blood glucose levels greater than 140 mg/ld. on at least two occasions. Interestingly, a few antipsychotic agents such as molindone (Type 1 antipsychotic), geodon and aripiprazole appear to have a slight weight reducing effect in previous studies. (Lieberman, 2004b).

Methodology

Databases resident at the CAM program allowed a retrospective analysis by comparing the baseline and three month follow-up of weight and body mass index of persons with mental illness who have recently used or who have not used psychotropic medication. This study originally intended to compare three groups of persons with diagnosed mental illness: 1) Persons using Type 1 antipsychotics; 2) persons using Type 2 antipsychotics; and 3) persons taking no antipsychotic medication. However, all individuals in the study who were taking Type 1 antipsychotics were also prescribed Type 2 antipsychotics leading to the decision to include them as one group. The final three participant groups for this research were: 1) persons taking Tpye 2 antipsychotics; 2) people taking both Type 1 and Type 2 antipsychotics; and 3) people taking no antipsychotices. Self-reported psychotropic use for the past 30 days was used for the categorization variable.

Data collection was from a retrospective chart review. The record review focused on past CAM consumers ages 18 and over who attended CAM during 2010-2011 for a period of three months. The data of 195 patients that were seen at CAM in Urbana, Ohio was obtained. The reviewed cases were randomly selected from all the patients who had height and weight

measurements noted at intake and three months after the use of antipsychotic medications. Seven patients were taken out of the study because they were less than 18 years old and one who had a diagnosis of mental retardation.

SPSS 17.0 was used for analysis. Since there was no single patient on Type 1 antipsychotic medication alone, there was an assigned Group in SPSS for consumers taking Type 1 and Type 2 antipsychotic medications. An independent t test analysis was used and compared the following: 1) Group with the cohort taking Type 2 antipsychotic medications only; 2) Group versus consumers who were taking medications other than antipsychotic medications; and 3) Type 2 versus consumers who were taking other medications. The General Linear Model (GLM) which approximates ANCOVA and compares means of three groups was also used. The dependant variables were BMI and change in BMI. Thefixed factor was group, and the covariates were age, race, and sex.

Use of inductive data

This study also included an examination of data from the Consumer Health Resource Group, LLC (Consumer Health Reports, 2011) that compiles uncensored user comments on the effects of taking different medications from people with a range of mental health diagnoses. Both a qualitative and quantitative analysis was conducted on data from patients taking two of the most widely prescribed Type 2 antipsychotic medications, olanzapine and risperidone, and patients taking the Type 1 antipsychotic medications haloperidol and chlorpromazine. In addition,information about how the reported effects of the antipsychotics interacted with the symptoms for which people were treated was reviewed. Respondents can record comments about a range of medicines which they are taking or have taken, including many drugs used in

psychiatry. Basic demographic information in separate fields, including t age, gender, diagnosis and the length of time they have been taking the drug was recorded and reviewed.

Variables for CAM study

The following variables were used to analyze the data from CAM records: 1) ID number; 2) Traumatic brain injury; 3) Medication listed at intake and prescribed treatment; 4) Group by Type 1 and Type 2; 5) Demographics: age, gender, race/ethnicity; education level; 6) DSM IV diagnosis; and 7) History of special education, borderline intellectual functioning, ADHD learning disorder; and comorbid medical or mental health conditions.

To compare prevalence of weight gain, hyperglycemia, hypercholesterolemia, hypertriglyceridemia, among consumers taking Type 1 or Type 2 antipsychotic medications. SPSS was used to run basic descriptive statistics independent t-test and ANCOVA (Analysis of Covariates). It is a General Linear Model analysis which compares the means between the three groups, making change in weight and BMI as dependant variables, group as fixed factor (medication Type 1 and Type 2, Type 2 or no medication) and making age, sex and race as covariates.

Results

Descriptive statistics and independent t test

Descriptive statistics for age are presented in Table 5. Males and females across all three groups were of similar ages (all independent t test, $p > 0.05$). The only group that was different in age for males was males not taking antipsychotics were significantly different from males taking antipsychotics ($p=0.046$). For females, those not taking antipsychotic were significantly younger then those taking Type 1 and 2 ($p=0.016$) and those taking Type 2 ($p=0.002$).

Descriptive statistics for weight and BMI are presented in Table 6. There was no significant difference in initial weight of males and females across the three groups. Initial BMI was significantly different for men on Type 2 then men on no antipsychotic medication ($p=0.002$). There was no significant difference in change in weight in males or females taking Type 2 antipsychotics and those taking Type 1 and 2 antipsychotic medications (all $p > 0.05$).

BMI and change in BMI in 3 months for individuals on antipsychotic medications

In order to determine if Type 2 was associated with greater initial and changes in BMI we compared the means of Group taking Type 1 and Type 2 antipsychotic medications versus Type 2 antipsychotic medications alone. Table 7 shows this. Nonsignificant effects of Group were seen on the BMI initially and after 3 months.

General Linear Model (GLM) analysis

GLM compares the means between the three groups. It can be used for ANOVA or ANCOVA (Analysis of Covariates). Change of Weight in 3 months by the use of antipsychotic Type 2 medications using a general linear model analysis making change in weight and BMI as dependant variables and making Group as fixed factor and making age, sex and race as covariates. Table 7 shows this GLM for the change in weight.

It can be seen from the table 7 a multivariate analysis of change in weight is carried out using GLM model with independent variables age, sex race, group. It shows significant ($p=<0.000$) effect across Group which is the fixed factor to that of change in weight in 3 months of using the antipsychotic medication. The R^2 is 67%, showing that the variables in the model explains the 67% of the variance in change in weight. The significance of sex can be explained by the fact that there is almost the same kind of weight gain in women on Type 1 and Type 2 antipsychotic medications and Type 2 alone, but in case of men there is a significant weight

increase with the use of Type 2 antipsychotic medications alone which can be explored further. More simply, women gained more weight then men.

Figure 1 and Figure 2 illustrates the results of the change in weight. There is a significant weight change in the groups being prescribed Type 1 and Type 2 antispsychotic medications and Type 2 antipsychotic medications alone compared to the patients' prescribed no antipsychotic medication.

A similar significant effect of medication group on the dependent variable change in BMI can be seen in table 8 using independent variables sex, age, race and group. Only Group was significant ($p=<0.0001$).

Discussion

Obesity policy versus guidelines

Some of the public health policies have been laid down to prevent the development of obesity. These policies can be helpful for patients who are taking Type 2 antipsychotic medications and experience weight gain. Some examples are given below:

- Mass media health promotion campaigns that emphasize healthful eating and physical activity patterns.
- Require and fund daily physical education and sports programs in primary and secondary schools.
- Develop culturally relevant obesity prevention campaigns for high-risk and low-income Americans.
- Require chain restaurants to provide information about calorie content on menus or menu boards and nutrition labeling on wrappers.

- Protect school food programs by eliminating the sale of soft drinks, candy bars, and foods high in calories, fat, or sugar in school buildings.
- Require health care providers to learn about behavioral risks for obesity and how to counsel patients about health-promoting behavior change.
- Use the National Nutrition Summit to develop a national campaign to prevent obesity.
- Develop a coordinated federal implementation plan for the Healthy People 2020 nutrition and physical activity objectives. as Type 2 antipsychotic medications have a tendency to cause weight gain.

All of these public health policies can help in patients on Type 2 antipsychotic medications if they follow them from day 1 of the there antipsychotic medication prescription (Papolos & Papolos, 2000).

Physical activity guidelines

The *Physical Activity Guidelines for Americans (*(DHHS, 2008a) indicates that regular physical activity reduces the risk of many adverse health outcomes. Some physical activity is better than none (DHHS, 2008a; CDC, 2011). Most health benefits occur with at least 150 minutes (2 hours and 30 minutes) a week of moderate intensity physical activity, such as brisk walking. The benefits of physical activity far outweigh the possibility of adverse outcomes (DHHS, 2008b).

Risks versus benefits of antipsychotic treatment

The quality of life associated with schizophrenia ranks among the worst of any chronic medical illness, and treatment with Type 2 antipsychotics may improve the quality of life for many patients. The greatest advantage of atypical antipsychotics is their ability to improve

cognition, since impaired cognition is now considered to be a fundamental feature of schizophrenia. Type 2 antipsychotics have been shown to significantly improve many aspects of cognitive function, including executive function, verbal fluency, attention, memory and learning impairment (Liberman, 2004b). Physicians must weigh the risks and benefits for each patient before beginning an antipsychotic treatment. The patient and the primary care provider must work together to outline potential risk factors and to carefully monitor risks during treatment.

In this small retrospective cross-sectional study, our findings are consistent with previous evidence in the literature, which suggests patients treated with Type 2 antipsychotic medication may be at increased risk of hyperlipidemia and hyperglycemia then people who were placed on second generation antipsychotic medication. So the question is whether to put the patient into the risk of development of metabolic side effects or to use antipsychotic medications Type 1? The decision depends on each case, the family history and risks of developing metabolic side effects for the patients.

The guidelines recommend routine monitoring of drug levels every 6 months. Routine monitoring of drug levels is required to gauge adequate dosing and to detect potential toxic levels that can lead to side effects and comorbidity. Referring the patient population on antipsychotic medications with abnormal glucose or lipid levels for a medical checkup. Encourage weight loss. Be alert of the possibility of diabetic ketoacidosis. Support moderate exercise and discourage smoking. Consider discontinuing the antipsychotic medications because it will resolve hyperglycemia and diabetes in some cases.

Limitations of the Current Study

The study is on the basis of 195 patients who were seen at CAM in Urbana. This is a small pool of patients, but it illustrates effects seen in larger clinical studies such as the CATIE

study. Only a three month period of medication use was studied, and the weight gain could even out with longer medication use.

Most number of patient population seen in the CAM clinic were caucasian and only 10% were black. So an even number of patients in the study may tell us the difference in the weight gain in terms of race.

The patient's weight gain could be due to several other reasons beside the antipsychotic medication itself. It could be the time period when the patients were enrolled in the study. Many patients were enrolled during holidays from December to April, 2010-2011. During this holiday mood people in general have a tendency to eat more then usual so the weight gain that was seen in patients on antipsychotic Type 2 medication could be related to the holiday mood and not due to the antipsychotic Type 2 medication itself, but more studies needs to be done in order to find out if antipsychotic medications have an effect on patients' behavior to eat more or craving for food. More studies needs to be done to find out the comorbidities or behavioral patterns of mildly intellectually disabled patients.

Recommendations

Prescribe Type 1 when possible

It shows Type 2 antipsychotic medications especially risperidone, seroquel, olanzepine, abilify increases the patients weight over the time and also in some cases have produced diabetes mellitus. It is a public health issue as being studied in multiple study trials because sheer number of people on it. People sometimes take it off label or on label especially in the elderly population. This concern should be addressed by using antipsychotic medications like Geodon, Invega or other new Type 2 antipsychotic medications which cause less weight gain.

Address weight gain by increasing the physical activity

Restlessness and confusion can be one of the side-effects with the use of antipsychotic medications especially if it is combined with alcohol and anxiolytic medications. With this confused state of mind and fall risk, patient's have a hard time to exercise or do any kind of physical activity. This might be the reason patients are at risk of gaining weight and developing the risk of diabetes mellitus. Certain programs should be developed for patients who are taking antipsychotic medications which could urge them to participate in some kind of exercise programs. Further studies should be done to develop a physical activity questionnaire for the patient population on antipsychotic medications.

Physicians should include a more public health perspective in their practice

Table 3 shows Type 1 medications are cheaper and in some cases is also offered as a $4 generic prescription compared to the antipsychotic medications. With the universal health insurance plan this should be an appropriate cost effective plan given the side-effects of the antipsychotic medications.

Annual revenues for all antipsychotic drugs are $14.6 billion (Wilson, 2009). Atypical antipsychotic drugs cost more than $13 billion in 2007, "nearly 5 percent of all U.S. drug expenditures" and are a major expenditure for Medicare Part D (Alexander, Gallagher, Mascola, Moloney, & Stafford, 2011). From a public health perspective cost effective treatment with the use of Type 1 antipsychotic medications rather than Type 2 antipsychotic medications should be encouraged however this can be decided on case by case basis.

Public health should add to the clinical perspective especially with universal health insurance coming up. Type 2 antipsychotic drug use can be associated with weight gain and development of insulin resistance and dyslipidemia. Treatment of this condition requires

coordination with the treating psychiatrist, close monitoring of their metabolic complications and the use of lifestyle intervention as well as adjuvant medical therapy as necessary. Each patient should be managed on a case by case basis with consideration of the degree of underlying psychiatric illness as well as previous responses to her antipsychotic agents and their individual risk factors for metabolic syndrome.

Listen to patients' feedback and concerns

Studies have found that clinicians ignore or minimize patient's complaints about the negative subjective effects of antipsychotics (Moncrieff et al., 2009). To improve patient's experience, doses of antipsychotics should be kept as low. Approaches that attempt to avoid or minimize the use of antipsychotics could also be explored further. Overall, prescribers need to take subjective effects of medications seriously and doctors and their patients should take into account the public health perspective regarding treatment such as the cost analysis and medication side effects. The patients need to be informed for every step of change taken during the treatment and the nature of these effects in order to make informed judgments about their use.

References

Alberti, K., Eckel, R., Grundy, S., Zimmet, P., Cleeman, J., Donato, K, & Smith Jr., S. (2009). Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation, 120*, 1640-1645.

Alexander, G., Gallagher, S., Mascola, A., Moloney, R., & Stafford, R. (2011). Increasing off-label use of antipsychotic medications in the United States, 1995-2008. *Pharmacoepidemiol and Drug Safety, 20*(2), 177-184.

Ascher-Svanum, H. (2005). Weight gain as a prognostic indicator of therapeutic improvement during acute treatment of schizophrenia with placebo or active antipsychotic. *Journal of Psychopharmacology, 19*(1), 37-49.

Barrett, A. (Ed.). (2004). *Diabetes: Antipsychotics*. Baltimore: Johns Hopkins.

Berrington de Gonzalez, A., Hartge, P., Cerhan, J. R., Flint, A. J., Hannan, L., MacInnis, R. J., & Thun, M. J. (2010). Body-mass index and mortality among 1.46 million white adults. *New England Journal of Medicine, 363*(23), 2211-2219. doi: 10.1056/NEJMoa1000367

Blackburn, G. (2001). Treatment approaches: food first for weight management and health. *Obesity Research, 9*(Suppl 4), 223S-227S.

Brannon, G. (2011). Schizoaffective Disorder. *Medscape Review.* Retrieved June, 2011, from http://emedicine.medscape.com/article/294763-overview.

Centers for Disease Control and Prevention (CDC). (2011). Physical Activity and Health. Retrieved Feb 16, 2011, from http://www.cdc.gov/physicalactivity/everyone/health/index.html.

Challoner, K. (2010). Toxicity, Neuroleptic Agents Follow-up. *Medscape Review.* Retrieved May, 2011, from http://emedicine.medscape.com/article/815881-overview.

Citromea, L., & Vreeland, B. (2009). Obesity and Mental Illness. In J. Thakore & B. Leonard (Eds.). *Review of Metabolic Effects of Psychotropic Drugs,* (pp. 25-46). Basel: Karger.

Centers for Medicare and Medicaid (CMS). (2011). Regulations and Guidance. Retrieved June, 2011, from www.cms.gov/home/regsguidance.asp.

Consumerhealthreports.org. (2011). Medications. Retrieved May, 2011.

Dart, H., & Colditz, G. (2010). Obesity: Economic Burden and Costs. *knol Beta.* Retrieved April, 2011, from http://knol.google.com/k/hank-dart/obesity-economic-burden-and-costs/1gvukm3swr4p3/9#.

Daumit, G. (2010). Physical Activity and Mental Health, *ACSM Select Symposium*: American Center for Sports Medicine.

DHHS. (2008a). 2008 Physical Activity Guidelines for Americans Summary. Retrieved March 2011, from http://www.health.gov/paguidelines/guidelines/summary.aspx.

DHHS. (2008b). Examining the relationships between excess body weight, health and disability. Washington, D.C.: U.S. Department of Health and Human Services Assistant Secretary for Planning and Evaluation; Office of Disability, Aging and Long-Term Care Policy.

Evans, W. D., Renaud, J. M., Finkelstein, E., Kamerow, D. B., & Brown, D. S. (2006). Changing perceptions of the childhood obesity epidemic. *American Journal of Health Behavior, 30*(2), 167-176. doi: 10.5555/ajhb.2006.30.2.167

Finkelstein, E., Ruhm, C., & Kosal, K. (2005). Economic causes and consequences of obesity. *Annual Review of Public Health, 26*(3), 239-257.

Gautam, S., & Meena, P. (2011). Drug-emergent metabolic syndrome in patients with schizophrenia receiving atypical (second-generation) antipsychotics. *Indian Journal of Psychiatry, 53*(2), 128-133. doi: 10.4103/0019-5545.82537

Grohl, J. (2010). Schizoaffective Disorder Treatment. Retrieved April, 2011, from http://psychcentral.com/disorders/sx4t.htm.

HealthyPeople.gov. (2011). Nutrition and Weight Status. Retrieved July 21, 2011, from http://healthypeople.gov/2020/topicsobjectives2020/overview.aspx?topicid=29.

Healy, M. (2011). Brain shrinkage seen in those taking antipsychotic medications, *The Los Angeles Times,* p. C1. Retrieved from http://articles.latimes.com/2011/feb/07/news/la-heb-antipsychotic-drugs-020711.

Jones, D., Macias, C., Barreira, P., Fisher, W., Hargreaves, W., & Harding, C. (2004). Prevalence, severity, and co-occurence of chronic physical health problems of persons with serious mental illness. *Psychiatric Services, 55*(11), 1250-1257.

Kushner, R., & Roth, J. (2003). Assessment of the obese patient. *Endocrinology Metabolism Clinics of North America, 32*(4), 915-933.

Levi, J., Vintner, S., Richardson, L., St. Laurent, R., & Segal, L. (2009). F as in Fat 2009: How Obesity Policies are Failing in America: Trust for America's Health.

Lieberman, J. (2004a). Metabolic Changes Associated With Antipsychotic Use. *Primary Care Companion Journal Clinical Psychiatry, 6*(Suppl 2), 8-13.

Lieberman, J. (2004b). Metabolic changes associated with antipsychotic use. *Journal of Clinical Psychology, 6*(suppl 2), 8-13.

Mandell, D. J., Unis, A., & Sackett, G. P. (2011). Post-drug consequences of chronic atypical antipsychotic drug administration on the ability to adjust behavior based on feedback in young monkeys. *Psychopharmacology (Berl), 215*(2), 345-352. doi: 10.1007/s00213-010-2147-6

McDevitt, J., Snyder, M., Miller, A., & Wilbur, J. (2006). Perceptions of barriers and benefits to physical activity among outpatients in psychiatric rehabilitation. *Journal of Nursing Scholarship, 38*(1), 50-55.

Moncrieff, J., Cohen, D., & Mason, J. (2009). The subjective experience of taking antipsychotic medication: a content analysis of Internet data. *Acta Psychiatrica Scandinavica, 120*(2), 102-111. doi: 10.1111/j.1600-0447.2009.01356.x

Motlagh, B., O'Donnell, M., & Yusuf, S. (2009). Prevalence of cardiovascular risk factors in the Middle East: a systematic review. *European Journal of Cardiovascular Prevention and Rehabiliation, 16*(3), 268-280. doi: 10.1097/HJR.0b013e328322ca1b

Nauret, R. (2009). Antipsychotic medications linked to unhealthy weight gain. *Psych Central.* Retrieved May, 2011, from http://psychcentral.com/news/2009/10/28/antipsychotic-medications-linked-to-unhealthy-weight-gain/9193.html.

Newcomer, J. W. (2007). Metabolic syndrome and mental illness. *American Journal on Managed Care, 13*(7 Suppl), S170-177.

NIMH. (2008). Mental Health Medications. In P. D. B. Science Writing (Ed.). Washington, D.C.: US Department of Health and Human Services, National Institutes of Health.

Ogden, C., Lamb, M., Carroll, M., & Flegal, K. (2010). Obesity and Socioeconomic Status in U.S. Adults *Data Briefs*. Atlanta, GA: National Center for Health Statistics, Centers for Disease Control and Prevention.

Papolos, J., & Papolos, D. (2000). Atypical Antipsychotics: Their Emerging Role in the Treatment of Early-Onset Bipolar Disorder. *The Bipolar Child: Vol. 5*. New York, NY: TheBipolarChild.com.

Puhl, R., & Heuer, C. (2010). Obesity stigma: important considerations for public health. *American Journal of Public Health, 100*(6), 1019-1028. doi: 10.2105/ajph.2009.159491

Ray, W. A., Taylor, J. A., Meador, K. G., Lichtenstein, M. J., Griffin, M. R., Fought, R., . . . Blazer, D. G. (1993). Reducing antipsychotic drug use in nursing homes. A controlled trial of provider education. *Archives of Internal Medicine, 153*(6), 713-721.

Robertson, J., Emerson, E., Gregory, N., Hatto, C., Turner, S., Kessissoglou, S., & Hallam, A. (2000). Lifestyle related risk factors for poor health in residential settings for people with intellectual disabilities. *Research in Developmental Disabilities, 21*(6), 469-486.

Scott, K. M., McGee, M. A., Wells, J. E., & Oakley Browne, M. A. (2008). Obesity and mental disorders in the adult general population. *Journal Psychosomatic Research, 64*(1), 97-105. doi: 10.1016/j.jpsychores.2007.09.006

Shaw, J., Sicree, R., & Zimmet, P. (2010). Global estimates of the prevalence of diabetes for 2010 and 2030. *Diabetes Research and Clinical Practice, 87*(1), 4-14. doi: 10.1016/j.diabres.2009.10.007

Sicras-Mainar, A., Navarro-Artieda, R., Rejas-Gutierrez, J., & Blanca-Tamayo, M. (2008). Relationship between obesity and antipsychotic drug use in the adult population: a longitudinal, retrospective claim database study in Primary Care settings. *Journal of Neuropsychiatric Disease and Treatment, 4*(1), 219-226.

Tarricone, I., Casoria, M., Gozzi, B., Grieco, D., Menchetti, M., Serretti, A., . . . Berardi, D. (2006). Metabolic risk factor profile associated with use of second generation

antipsychotics: a cross sectional study in a Community Mental Health Centre. *BioMed Central Psychiatry, 6*(1), 11. doi: 10.1186/1471-244x-6-11

Thompson, D., Edelsberg, J., Kinsey, K. L., & Oster, G. (1998). Estimated economic costs of obesity to U.S. business. *American Journal of Health Promotion*, *13,* 120-127.

Ussher, M., Stanbury, L., Cheeseman, V., & Faulkner, G. (2007). Physical activity preferences and perceived barriers to activity among persons with severe mental illness in the United Kingdom. *Psychiatric Services, 58*(3), 405-408.

Venes, D. (Ed.). (2010). *Taber's Medical Dictionary Online*. Charlottesville, VA F.A. Davis; Unbound Medicine, Inc.

Wilson, D. (2009, Oct 27). Rapid Weight Gain Linked to Antipsychotic Drugs, *The New York Times,* p. 1. Retrieved from http://www.nytimes.com/2009/10/28/business/28psych.html.

Zagaria, M. (2011). Antipsychotic-associated Metabolic and Cardiovascular Risks. *Practice Management.* Retrieved March, 2011, from http://www.nppracticemgt.com/columns/details/antipsychotic-associated-metabolic-and-cardiovascular-risks-monitoring-and-/.

Appendix A

Glossary

Akathisia: An inability to remain motionless or sit still.

Akinetic: Absence or lack of movement.

BMI: Body Mass Index (BMI) is a number calculated from a person's weight and height.. Abnormal metabolic levels and BMI are defined by the National Cholesterol Education Program (NCEP) and World Health Organization (WHO) criteria as follows: 1) an abnormal BMI between 25 and 29.9 for overweight and equal to or greater than 30 for obesity; 2) an abnormal blood glucose level equal to or greater than 110 mg/dl (equal to or greater than 126 mg/dl for diabetes); 3) an abnormal blood cholesterol level equal to or greater than 200 mg/dl; 4) an abnormal blood triglyceride level equal to or greater than 150 mg/dl (Tarricone, 2006).

Dysphoria: An unpleasant or uncomfortable mood, such as sadness.

Dystonia: Sustained muscle contractions that cause twisting and repetitive movements or abnormal postures.

EPS: Extrapyramidal symptoms (EPS) are various movement disorders such as acute dystonic reactions, or akathisia suffered as a result of taking dopamine antagonists, usually antipsychotic (neuroleptic) drugs.

Hypertriglyceridemia: An increased blood triglyceride level; a possible risk factor for cardiovascular disease.

Metabolic Syndrome: Metabolic syndrome is a condition characterized by impaired glucose regulation, diabetes type I, insulin resistance, raised arterial pressure $\geq$ 160/90 mm Hg,

raised plasma triglyceride levels, raised LDL, cholesterol level, and/or BMI > 30 kg/m2, and microalbuminuria (Alberti, 2009).

Tardive Dyskinesia: A condition that is characterized by repetitive, involuntary, purposeless movements, such as grimacing, tongue protrusion, lip smacking, puckering and pursing of the lips, and rapid eye blinking.

Type I (Typical) Antipsychotic Medications: Haldol, chlorpromazine, Loxapine and thorazine, are the most commonly known typical antipsychotic medications.

Type II (Atypical) Antipsychotic Medications: The newer antipsychotic medications such as Zyprexa, olanzepine, seroquel, risperidone, Latuda, fanapt and abilify are commonly prescribed Type 2 antipsychotic medications.

Unless otherwise cited all definitions cited verbatim, Venes, 2010.

Appendix B

Table 1: Effects of obesity on physical health

Cardiovascular
- Hypertension
- Congestive heart failure
- Cor pulmonale (Pulmonary Hypertension)
- Coronary artery disease

Endocrine
- The metabolic syndrome
- Type 2 diabetes
- Dyslipidemia (Cholesterol problems)

Gastrointestinal
- Gastroesophageal reflux disease (GERD)
- Cholelithiasis (Gall Stones)

Genitourinary
- Pregnancy complications

Musculoskeletal
- Osteoarthritis (knees, hips)
- Low back pain

Neurologic
- Stroke

Psychological
- Depression/low self esteem

Respiratory
- Obstructive sleep apnea
- Asthma

(Kushner and Roth , 2003)

Table 2: Type 1 Antipsychotic medications prescribed for and side effects

Type 1	Brand Names	Prescribed For	Known Side Effects
Chlorpromazine	Thorazine	Schizophrenia, vomiting	Akathisia,
Fluphenazine	Prolixin	Schizophrenia	Parkinsonism
Haloperidol	Haldol	Schizophrenia	EPS
Loxapine	Loxitane	Schizophrenia	Weight Gain
Molindone	Moban	Schizophrenia	NMS
Perphenazine	Trilafon	Schizophrenia	TD
Pimozide	Orap	Schizophrenia	EPS
Thiothixine	Navane	Schizophrenia	EPS
Trifluopromazine	Vesprin	Schizophrenia	EPS

NMS=Neuromalignant syndrome, EPS= Extrapyramidal side effects, TD=Tardive Dyskinesia

Table 3: Type 2 Antipsychotic medications prescribed for and side effects

Type 2	Brand Name	Prescribed For	Known Side Effects
Aripiprazole	Abilify	Schizophrenia, Bipolar	Wt. gain, Akasthesia
Asenapine	Saphris	Schizophrenia, Bipolar	Akasthesia
Clozapine	Clozaril	Schizophrenia	Sedation, Agranulocytosis
Lurasidone	Latuda	Schizophrenia	Akasthesia
Olanzepine	Zyprexa	Schizophrenia, Bipolar	Wt. gain, Akasthesia
Paliperidone	Invega	Schizophrenia	Wt. gain, Akasthesia
Risperidone	Risperdal	Schizophrenia, Bipolar	Wt. gain, breast enl, Akasthesia
Quetiapine	Seroquel	Schizophrenia, Bipolar, Insomnia	Wt. gain, Akasthesia
Ziprasidone	Geodon	Schizophrenia	Wt. gain, Akasthesia

Table: 4 Cost Analysis for Antipsychotic medications

Type	Medication	Dose	30 day supply	Cost without Insurance	Cost with Medicaid	Cost with Anthem	$4 plan
II	Abilify	2,5,10,15	30	$450	$2.00	$10	No
II	Abilify	20,30	30	$600	$2.00	$20	No
II	Seroquel	5,100	30	$500	$2.00	$10	No
II	Seroquel	200, 400, 600	30	$930	$2.00	$20	No
II	Olanzepine	5,10,20	30	$275	$2.00	$15	No
II	Risperidone	0.5,1,2,3, 4	30	$250	$0.00	$10	No
I	Haloperidol	5, 10	30	$25-$50	$0.00	$10	Yes
I	Prochlorperazine	5,10	30	$25	$0.00	$10	Yes
I	Loxapine	5, 10, 50	30	$25	$0.00	$10	Yes

Table 5: Demographics

Age

Type 1 & 2 Antipsychotics						**Type 2 Antipsychotics**						**No Antipsychotics**					
Males N=30		Females N=39		Total N=69		Males N=85		Females N=41		Total N=126		Males N=27		Females N=39		Total N=66	
x	sd	X	sd	x	sd	x	sd	x	sd	x	sd	x	sd	x	sd	x	sd
35.5	10.4	34.5	9.3	35.5	10.0	37.0	10.6	36.4	10.6	36.8	10.6	32.4	9.41	29.3	9.3	30.5	9.4

X= mean and sd= standard deviation.

Overall Total

x	sd
34. 6	10.6

(Where x= Mean and sd= Standard Deviation).

Table 6: Weight and BMI Data (mean + sd)

Antipsychotic Medication	**None**	**Type 1 & 2**	**Type 2**
	N=66 (M = 27, F = 39)	N=69 (M =30 , F =39)	N=126 (M =85 , F =41)
Initial Weight (kg)			
M	149.3 ± 14.1	153.4 ± 13.3	155.4 ± 15.6
F	141.4 ± 18.3	156.6 ± 17.2	153.2 ± 15.6
Overall	145.5 ± 16.3	153.5 ± 15.2	154.4 ± 15.6
3 month weight (kg)			
M	149.6 ± 14.1	162.1 ± 14.6	164.1 ± 16.5
F	141.5 ± 18.3	167.4 ± 18.0	164.2 ± 10.1
Overall	145.5 ± 16.3	164.5 ± 15.2	164.5 ± 13.3
Weight change (kg)			
M	0.30 ± 0.60	6.7 ± 3.1	8.7 ± 4.5
F	0.08 ± 0.42	10.8 ± 1.2	10.9 ± 1.2
Overall	0.05 ± 0.35	8.4 ± 6.2	9.2 ± 10.3
Initial BMI			
M	22.5 ± 1.9	24.7 ± 1.7	24.0 ± 2.2
F	22.1 ± 2.5	26.2 ± 2.3	25.3 ± 2.3
Overall	23.8 ± 2.2	25.2 ± 2.0	25.0 ± 2.2
3 month BMI			
M	22.5 ± 1.9	25.6 ± 1.8	26.9 ± 2.4
F	22.1 ± 2.5	26.4 ± 2.2	27.1 ± 2.2
Overall	23.8 ± 2.2	26.0 ± 2.0	27.0 ± 2.3
BMI Change			
M	0.0 ± 0.0	0.9 ± 0.1	2.9 ± 0.2
F	0.0 ± 0.0	0.2 ± 0.1	2.1 ± 0.1
Overall	0.0 ± 0.0	0.8 ± 0.0	2.0 ± 0.1

Table 7: Using Independent t-test

Change in Initial BMI and change in BMI in 3 months:

	Group	N	Mean	Std. Deviation	Std. Error Mean
BMI initial	Type 1 & type 2	43	25.22	2.022	.308
	Type 2 only	83	24.99	2.408	.264
BMI 3months	Type 1 & type 2	43	27.226	2.0545	.3133
	Type 2 only	83	27.001	2.4977	.2742

Independent Samples Test

	Levene's Test for Equality of Variances		t-test for Equality of Means						
	F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval	
								Lower	Upper
BMI initial	1.214	*.273	.526	124	.600	.226	.429	-.624	1.076
			.556	99.023	.579	.226	.406	-.580	1.032
BMI 3months	1.701	*.195	.507	124	.613	.2244	.4429	-.6522	1.1009
			.539	100.703	.591	.2244	.4163	-.6015	1.0503

Table 8: GLM analysis

Dependent Variable:Change in Wt.

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	3893.793[a]	5	778.759	79.479	0
Intercept	58.795	1	58.795	6.001	0.015
Sex	61.728	1	61.728	6.3	0.013
Age	0.19	1	0.19	0.019	0.889
Race	23.162	1	23.162	2.364	0.126
Group	3415.002	2	1707.501	174.266	0
Error	1832.27	187	9.798		
Total	13262	193			

a. R Squared = .680 (Adjusted R Squared = .671)

Table 9: GLM Analysis

Dependent Variable: Change in BMI

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	103.308[a]	5	20.662	14.918	.000
Intercept	11.928	1	11.928	8.612	.004
Sex	.088	1	.088	.063	.802
Age	.770	1	.770	.556	.457
Race	1.052	1	1.052	.760	.385
Group	85.458	2	42.729	30.851	*.000
Error	258.997	187	1.385		
Total	773.470	193			
Corrected Total	362.305	192			

Figure 1: Medication use and change in weight in a period of 3 months

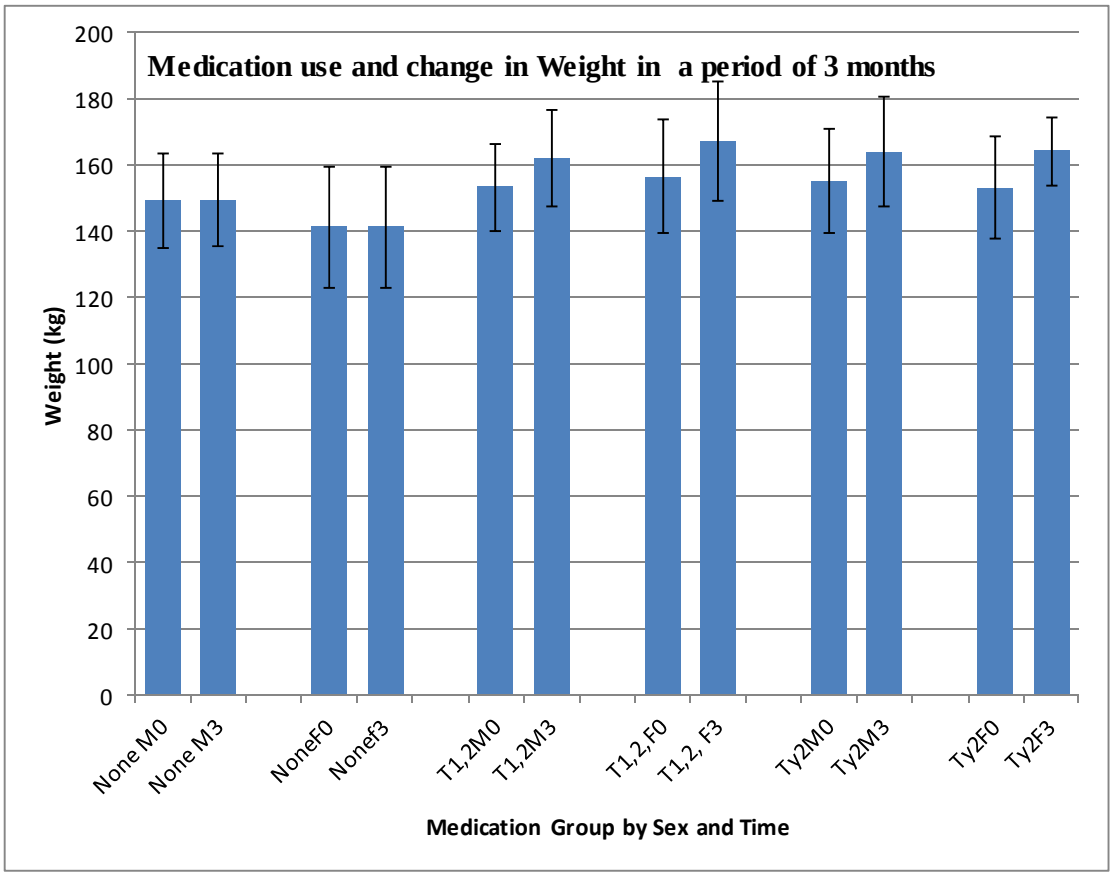

Figure 2: Change in Weight with the medication